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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,048	09/16/2003	Ming-Derg Lai	LAIM3006/REF	2552

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EXAMINER	
GUZO, DAVID	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 08/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/663,048	LAI ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Applicant's election without traverse of Group I, Claims 1-18 in the reply filed on 7/20/05 is acknowledged.

Non-elected Claims 19-36 have been cancelled.

Specification

A substitute specification (excluding the claims) in proper idiomatic English and in compliance with 37 CFR 1.52(a) and (b) is required. The substitute specification filed must be accompanied by a statement that it contains no new matter.

35 USC 102 Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 8, 10, 12, 13 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Pasquini et al.

Applicants claim a DNA vaccine containing a tumor-associated gene and a cytokine gene made by incorporating into a vector having a suitable promoter (which can be a mammalian expression promoter having a CMV promoter) or translation regulatory sequence at least: a fragment of a tumor-associated gene; and a fragment of

cytokine gene (which can be GM-CSF). The tumor associated gene and cytokine gene are constructed into a fusion gene controlled by the same promoter.

Pasquini et al. (Gene Therapy, April 2002, Vol. 9, pp. 503-510, see whole article, particularly the Abstract, Figures 1-6, pp. 504-506) recites a DNA vaccine containing a tumor associated gene sequence (from the complementarity-determining regions of the leukemic clone-specific immunoglobulin heavy chain) as a fusion product with the mouse sequence encoding the cytokine GM-CSF. The nucleic acid sequence is under control of a CMV promoter (in the context of the pcDNA3 vector) with the cytokine gene in front of the tumor associated gene sequence. It is noted that the pre-B cell leukemia is a blood born non-solid tumor. Therefore, Pasquini et al. teaches the claimed invention.

Claims 1-3, 5, 8, 10-12 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Glorioso et al. (US 5,998,174).

Applicant's invention is as described above. Additionally, applicants recite that the DNA vaccine comprising the cytokine gene comprises the "mature" gene segment of IL-2 (claim 11) and that the tumor-associated gene and the cytokine gene are two independent genes controlled by two different independent promoters (claim 14).

Glorioso et al. (see whole document, particularly Fig. 10D; paragraph bridging columns 4-5; columns 11-15) recites HSV multigene expression vectors which comprise a gene encoding a tumor-associated antigen and a cytokine which can be IL-2 or GM-CSF, etc. wherein each gene can be under control of independent promoters (one or

more of which can be a CMV promoter. With regard to claim 11 reciting a "mature" gene segment of IL-2, applicants do not define in the specification, what is meant by this terminology. It is assumed that applicants mean a gene segment which encodes the mature (processed) IL-2 protein. Since Glorioso et al. teaches a recombinant HSV vector which expresses the IL-2 gene, it must be assumed, absent evidence to the contrary, that said gene comprises a mature IL-2 gene segment. Glorioso et al. therefore teaches the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 8, 12, 14-15, 17 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Cotten et al. (US 6,797,506).

Applicant's invention is as described above. In addition, applicants recite that the DNA vaccine contain an IRES element (claim 4), that the tumor-associated gene and the cytokine gene are two separate genes regulated by a promoter and IRES element (claim 15).

Cotten et al. (see whole document, particularly columns 5-7) recites a recombinant adenovirus vector (CELO virus) comprising expression cassettes capable

of expressing a tumor-associated gene and a cytokine gene (in any order) wherein the promoter can be a CMV or RSV LTR promoter and wherein the genes encoding the tumor-associated gene and the cytokine can be independent genes under control of separate promoters or under control of one promoter and an IRES element and wherein the vector can be administered by subcutaneous or intramuscular injection. Cotton et al. therefore teaches the claimed invention.

35 USC 103(a) Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glorioso et al. or Cotten et al., either in view of Hand-Zimmermann et al. (US Pub. No. 2002/0193329).

Applicants claim a DNA vaccine containing a tumor-associated gene and a cytokine gene made by incorporating into a vector having a suitable promoter or translation regulatory sequence at least: a fragment of a tumor-associated gene; and a fragment of cytokine gene wherein the tumor-associated gene is a truncated segment of the oncogene neu and wherein the N'-neu gene encodes the extracellular domain of neu protein. It is noted that applicants' use of the term "N'-neu" to denote the neu oncogene is confusing. Applicants do not appear to indicate, in the specification, that "N'-neu" denotes anything except a sequence encoding the neu protein or the extracellular domain of neu protein and this is how the examiner will interpret this claim limitation. The term "N'-neu" does not appear to be defined in the prior art.

Glorioso et al. and Cotten et al. are applied in the above 35 USC 102 rejections. Glorioso et al. and Cotten et al. do not teach that the tumor-associated gene is a oncogene such as neu or a sequence encoding the extracellular domain of neu.

Hand-Zimmermann et al. (See whole document, particularly Figs. 3-4, paragraphs [0009], [0309]-[0313] teaches that the neu oncogene (also known as HER-2/neu or p185) is well characterized and is found to be overexpressed and amplified in many different cancers in humans. Hand-Zimmermann et al. also teaches that the extracellular domain of the neu protein, when expressed from DNA vaccines mediates tumor protection in mice.

The ordinary skilled artisan, seeking to choose a tumor associated gene to be expressed in the DNA vaccine vectors disclosed by Glorioso et al. or Cotten et al., would have been motivated to choose the neu oncogene and specifically the extracellular domain of the neu protein because Hand-Zimmermann et al. teaches that the neu gene is a well characterized human oncogene associated with a wide variety of human cancers and that expression of the extracellular domain of the neu protein confers protection for tumor challenge in mice. It would have been obvious for the ordinary skilled artisan to choose the neu oncogene because Hand-Zimmermann et al. teaches that the neu is well characterized and is involved in a wide variety of human cancers and hence would be an obvious choice for the ordinary skilled artisan to include in the DNA vaccine vectors disclosed by Cotten et al. or Glorioso et al. Given the teachings of the cited prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

35 USC 112, 2nd Paragraph Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 9, 10, 16, 17 (and dependent claims) are vague in that applicants do not place articles before nouns in the claims. For example, in Claim 1, applicants recite "containing tumor-associated gene and cytokine gene...". Proper grammar requires an article such as "a" prior to the "tumor-associated gene", etc.

Claim 1 is vague and contradictory in that it recites a DNA vaccine containing a **tumor-associated gene** and a **cytokine gene**, but then recites that the vector can contain only **a fragment** of said genes.

Claim 2 is vague in the recitation of a "mammalian expression promoter" because it is unclear if applicants are reciting a promoter operable in mammalian cells or a promoter found in expression vectors or a promoter from a mammalian gene, etc.?

Claim 3 is vague in that applicants recite promoters comprising "CMV, PSV or LTR". The terms recited by applicants are not promoters but instead are viruses or portions of viruses.

Claims 9 and 16 are vague in the recitation of the term "N neu gene". The specification discloses the term "N'-neu gene" and it appears that applicants neglected to include the "'-" after "N". However, even if applicants correct this, the term "N'-neu" is not defined in the specification or in the prior art and it is unclear what this term denotes. The term could refer to the neu gene or to the extracellular domain of the neu gene or to some other form or variant of the neu gene, etc.

Claim 11 is vague in the recitation of the term "the mature gene segment of Interleukin-2". The term "mature" is usually used to denote the mature (i.e. processed

by the cell) form of the protein and its' use with regard to a nucleic acid sequence is unclear.

Claim 12 is vague in the recitation of the phrase "wherein the genes contained in..." because this language is not grammatically correct and is confusing. Redrafting the claim to recite "wherein the genes contained therein" would be remedial.

Claim 15 is vague in that there is no antecedent basis for the term "said IRES segment" in claim 1.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo
August 21, 2005

DAVID GUZO
PRIMARY EXAMINER